REMARKS

This Response is filed to the Office Action dated March 28, 2001. The Examiner has rejected claims 1-20, 26-29 and 32-54 under 35 U.S.C. §102(b) as being anticipated or, alternatively, under 35 U.S.C. § 103(a) as being obvious in light of prior art, citing primarily US Patent 3,928,594 (Cook) in both cases and further referring to Yang et al. (Anesthesiology 88:334-339) to show the state of this art. The Examiner has objected to claims 30 and 31 as being dependent upon a rejected base claim, in this case claim 29, but has indicated that these claims would be allowable if rewritten in independent form. Claims 21-25 were deemed allowable over the prior art record. For the reasons detailed below, Applicants request that these rejections be withdrawn and claims 1-33 and 55 be allowed to issue. Claims 34-54 are cancelled without prejudice to the prosecution of this subject matter in separate patent applications. Applicants have added new claim 55.

I. Objections

The Examiner has objected to claims 30-31 as being dependent upon the rejected base claim 29, and further indicates that said claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. As we believe that claim 29 was improperly rejected (see below), Applicants respectfully request that the Examiner's objection to these claims now be withdrawn and the claims be allowed to issue.

II. Rejections

The Examiner rejects claims 1-20, 26-29 and 32-54 under 35 U.S.C.§102(b) as being anticipated by U.S. Patent 3,928,594 (Cook), or in the alternative, 35 U.S.C.§103(a) as being obvious in light of this same patent.

Applicants respectfully disagree with the Examiner's rejections on both grounds.

Rejections under 35 U.S.C. §102(b)

The Examiner has rejected claims 1-20, 26-29 and 32-54 under 35 U.S.C.§102(b) as being anticipated by U.S. Patent 3,928,594 (Cook), stating that: "Cook discloses a method of diagnosing the intensity of pain in a patient comprising determining the amount of cholinesterase in a biological sample from the patient." Applicants respectfully assert that this characterization is incorrect in that it attributes a level of detail and comprehensiveness to the Cook patent that simply is not found in the disclosure. In contrast to the Examiner's expansive summary, the Cook patent merely describes a method for treating the signs and symptoms associated with demyelination disorders, specifically multiple sclerosis, using a specific cholinesterase reactivator of the oxime class. This method has nothing to do with Applicants' method of detecting pain using a measurable marker. Cook is primarily concerned with alleviating pain and implicitly assumes its presence.

Admittedly, Cook does mention in passing (Column 6, lines 13 and 14) that its methods may also be useful in the treatment of pain, and elsewhere in the application states that pain perception may be altered through the application of these compounds (Column 4, line 36). Based upon these mere passing suggestions, the Examiner contends that the Cook patent "discloses a method of diagnosing the intensity of pain in a patient comprising determining the amount of cholinesterase in a biological sample from the patient". However, the Examiner provides little direct evidence to support his conclusion, likely because it simply does not exist within the Cook patent. Specifically, the lines in column 2 cited by the Examiner indicate that Cook, on the basis of responses observed in humans to electrical stimulation of the dorsal surface of the spinal cord, believes that these responses may be achieved through renormalization of "an imbalance in cholinergic and adrenergic activity" (Column 2, lines 52 and 53), but this is not supported by any direct evidence in the Cook patent or elsewhere. In fact, it is now well known in the art that a plethora of neurotransmitter systems are involved in pain responses, the relative function of any number of which could be altered by electrical stimulation, depending upon the intensity of the signal, its duration, and its site of administration. (See Forsman et al. (J. Neurophysiol 39:534-546) or Wilson and Yaksh (Anaesth Intensive Care 8:248-256) for reviews of the field that are roughly contemporaneous with Cook). Thus, in the absence of direct evidence by Cook, there is little support to sustain Cook's contention that pain is due to an imbalance in cholinergic activity and not to imbalances in any number of other neurotransmitters as well. Moreover, even if one accept Cooks

"belief" that the pain his method alleviates results from an imbalance of cholinergic or adrenergic activity, there is no enabling description of how one might detect such an imbalance.

As expressed in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1997), "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Furthermore, "The identical invention must be shown in as complete detail as is contained in the ... claim." (*Richardson v. Suzuki Motor Co. Ltd.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920) In the present instance, for the pending claims to be anticipated, either Cook or Yang et al. must teach a method for the diagnosis of pain similar in nature and function to those of the instant claimed invention. A careful reading of the Cook patent fails to provide any evidence to one skilled in the art that Cook teaches any method for diagnosing pain through the measurement of any biological compound in any tissue, and certainly provides no evidence for enablement. A similar examination of the cited Yang reference (Yang et al. (Aneshtesiology 88:334-339)) also fails to uncover evidence of diagnosis of pain through the measurement of any biological molecules in patient samples. YRather, the Yang study utilizes the potentially subjective visual analog pain score (VAS) as a measure of pain intensity in subjects and primarily focuses on the relief of pain rather than its detection using a marker. Thus, Applicants submit that neither the independent claims 1, 9 16, 21, 26 and 29 nor the dependent claims 2-8, 10-15, 17-20, 21-25, 27-28 and 30-33, all of which

deal with methods of diagnosing pain or stress in patients by determining the amount of a marker or markers in a biological sample or samples obtained from said patients wherein said marker or markers correlate with the perception of pain or stress, are anticipated by either Cook or Yang et al., and therefore respectfully request that rejections of claims 1-33 on the basis of 35 U.S.C. §102 (b) be withdrawn.

Rejections under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-20, 26-29 and 32-54 under 35 U.S.C.§102(b) as being obvious, again citing U.S. Patent 3,928,594 (Cook) and secondarily Yang et al. Again, the critical issue here is whether either of the cited references teach a method of diagnosing the intensity of pain or stress in a patient. If neither of the references teaches such a method, it is impossible to combine or alter them in an obvious manner to arrive at the present invention. As stated above, a thorough review of both cited references fails to uncover any evidence that either teaches such methods. Thus, Applicants respectfully traverse this rejection and assert that it would not have been obvious to one skilled in the art to assay serum cholinesterase or any other marker in biological samples as a means of determining the intensity of pain or stress being experienced by a patient.

According to the MPEP §2141, the "Basic Considerations Which Apply to Obviousness Rejections" are:

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention and

(D) Reasonable expectation of success in the standard with which obviousness is determined. (Reference omitted.)

Applicants assert that (i) neither Cook nor Yang et al. teach or suggest the desirability of the assay of serum cholinesterases or other markers as a means of determining the intensity of pain or stress experienced by a patient nor, (ii) do they provide one skilled in the art with the necessary "reasonable expectation of success" to do so. This assertion is supported by the arguments that follow.

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the difference between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The relevant inquiry is whether the prior art both suggests the

invention and provides one of ordinary skill in the art with a reasonable expectation that the suggestion would work. *In re O'Farrell*, 853 F.2d 1549, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be found in the prior art and not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991).

In the present instance, the proper inquiry is whether, in view of the cited art, it would have been obvious to one of ordinary skill in the art to measure serum cholinesterase activity or other markers that correlate with pain as a means of determining the intensity of the pain being experienced by the patient. Cook is non-responsive to this question because it fails to describe the measurement of any biological markers. Yang et al., through its use of the potentially subjective visual analog scale to quantify the pain being experienced by patients does address pain intensity, but, because it uses just the sort of subject measurement the present invention is intended to avoid, Yang et al. actually teaches away from the claimed instant invention. Thus, Applicants submit that neither the independent claims 1, 9 16, 21, 26 and 29 nor the dependent claims 2-8, 10-15, 17-20, 21-25, 27-28 and 30-33, are obvious from either Cook or Yang et al., and therefore respectfully request that rejections of claims 1-33 on the basis of 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

Based on the foregoing remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Applicants believe a fee in the amount of $55 is required for a one month extension of time under 37 C.F.R. 1.17(a)(1) and, accordingly, a check in that amount is enclosed. Applicants believe no additional fees are due. Should any additional fees be due for this or any other communication, the Commissioner is hereby authorized to charge Deposit Account Number 02-4377. Two copies of this page are enclosed.

Respectfully submitted,

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